

NON-TECHNICAL ABSTRACT

Gene therapy represents a potential novel treatment for patients with HIV-1 infection. The term "intracellular immunization" has been used to describe the process of putting a gene into a cell which would make that cell resistant to an infectious agent, such as HIV-1. HIV-1 primarily infects CD4+ T lymphocytes and monocytes, macrophages, dendritic cells and microglial cells in the brain. Each of these cell types comes from stem cells in the bone marrow. Theoretically, putting an HIV-resistance gene into a patient's bone marrow stem cells and transplanting that marrow back into the patient could lead to the production of cells which resist HIV infection. If a patient's cells could be engineered to be resistant to supporting the growth of HIV-1, disease progression may be slowed or prevented.

Our pre-clinical studies have tested a gene, an **RRE decoy**, which inhibits the growth of the AIDS virus. We have shown that the RRE decoy can be inserted into cells from human bone marrow, the RRE decoy is made in the cells, does not interfere with the normal activities of the cells and the RRE decoy inhibits HIV from growing in the cells by >99%.

We now propose to test whether the RRE decoy gene can be put into bone marrow cells from patients with HIV-1 infection and then be made in blood cells of the patient and allow the cells making the RRE decoy to survive better in the patients. Although we do not think that this initial study is likely to have a significant medical benefit for the patient, we believe that it is safe and may provide useful information for progressing to potential beneficial treatments for AIDS.